

AWARD NUMBER: W81XWH-14-1-0466

TITLE: Clonal Evaluation of Prostate Cancer by ERG/SPINK1 Status to Improve Prognosis Prediction

PRINCIPAL INVESTIGATOR: Scott A. Tomlins, M.D., Ph.D.

CONTRACTING ORGANIZATION: Regents of the University of Michigan  
Ann Arbor, MI 48109

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14. ABSTRACT Prostate cancer is commonly multiclonal, meaning that most men with prostate cancer have multiple, genetically distinct cancers. Pathologists cannot assess clonality by routine microscopic evaluation, and hence multiclonality is not incorporated into routinely reported pathological parameters, such as the number of cores with cancer. Given the importance of routine pathological parameters in prostate cancer prognosis, the potential to refine these parameters through assessing multiclonality represents a major opportunity. Hence, the objectives of this proposal are to utilize dual ERG/SPINK1 immunohistochemistry (IHC)—which can identify clonal, mutually exclusive molecular subtypes—to assess the frequency of multiclonality in key clinical scenarios at biopsy and resection and its impact on prognostic parameters. We have published initial findings from this proposal that confirm multiclonality in key diagnostic scenarios and our ongoing work supports relevant multifocality in other important scenarios.					
15. SUBJECT TERMS Multiclonality, ERG, SPINK1, immunohistochemistry, active surveillance, prostate biopsy, prostatectomy					
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**INTRODUCTION:**

Prostate cancer is commonly multiclonal (also referred to as multifocal), meaning that more than 80% of men with prostate cancer actually have multiple, genetically distinct cancers in their prostate. Pathologists cannot assess focus clonality by routine microscopic evaluation, and hence multiclonality is not incorporated into routinely reported pathological parameters, such as the number of biopsy cores with cancer. Given the importance of routine pathological parameters in predicting the extent and behavior of prostate cancer, the potential to refine these parameters through assessing multiclonality represents a major opportunity. Hence, the objectives of this proposal are to utilize dual ERG/SPINK1 immunohistochemistry (IHC)—which can identify clonal, mutually exclusive molecular subtypes—to assess the frequency of multiclonality in key clinical scenarios at biopsy and resection. Secondly, we aim to determine the impact of multiclonality on the ability of pathological parameters at biopsy to predict pathology at resection or outcome after resection. We hypothesized that incorporating multiclonality by IHC evaluation will improve the predictive ability of pathological parameters, and in doing so, will increase the number of men eligible for active surveillance, enhancing the well-being of men with prostate cancer through minimizing over-treatment and treatment-related side effects.

**KEYWORDS:**

Multiclonality, ERG, SPINK1, immunohistochemistry, active surveillance, prostate biopsy, prostatectomy

**ACCOMPLISHMENTS:****What were the major goals of the project?:***SPECIFIC AIMS*

- 1) Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC.
- 2) Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy.
- 3) Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction.

**What was accomplished under these goals?**

To accomplish these aims, we developed a tri-institutional collaboration between Drs. Tomlins (PI; University of Michigan [UM]), Larry True (University of Washington [UW]) and Juan Miguel Mosquera (Weill Cornell Medical College). Our proposed statement of work was essentially the same for each site, with the exception of 100 cases to be scanned at the University of Michigan and reviewed by Drs. True and Mosquera (original UM, UW and WCMC statements of work Specific Aim 1.4.c). Likewise, data will be transferred from UW and MCMC to UM for analysis in the third year of the award (UM, UW and WCMC statements of work, Specific Aim 2.3 and 3.3). Hence, progress at each site is reported using the UM statement of work. Progress is described in italics.

Specific Aim 1: Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC.

- 1) Obtain study IRB and DoD HRPO approval (months 1-2).

*All work sites (UM, UW and WCMC) have now received local IRB and DOD HRPO approval.*

*Overall, this task is approximately 100% completed.*

- 2) Retrospectively identify and review eligible cases (months 3-18)
  - a. Retrospectively identify and review biopsy cases (n=100) from pathology database with discontinuous involvement (months 3-18).
  - b. Retrospectively identify and review biopsy cases (n=100) from pathology database with Gleason score 6 or 3+4=7 and 2-5 positive cores (months 3-18).
  - c. Retrospectively identify and review cases (n=134) from pathology database with Gleason score 3+4=7 at prostatectomy (months 3-18).

*After local IRB and HRPO approval, Dr. Tomlins has performed a retrospective search through the UM institutional prostate cancer tissue bank, identifying and reviewing 32 discontinuously involved prostate biopsy cores. Upon evaluation of an additional 103 cases to evaluate for potential discontinuous involvement that fulfilled the following clinical criteria: 1) Gleason score 6 or 3+4=7 on biopsy; 2) 1-5 cores involved on biopsy; and 3) at least one core >50% involvement, we identified an additional 8 cases. Importantly, this is the group of patients where potential discontinuous involvement would drive clinical management. Review of these cases is 100% complete.*

*Likewise, we have identified a total of 277 cases to evaluate for multiclonality in multiple positive cores that fulfilled the following clinical criteria: 1) Gleason score 6 or Gleason 3+4=7 on biopsy; 2) 1-5 cores involved on biopsy and the patient underwent prostatectomy at UM. Review of these cases is complete..Lastly, we have identified 738 cases to evaluate for multiclonality at prostatectomy that fill the following clinical criteria: 1) Gleason score 3+4=7 or 4+3=7 with at least 3 yrs PSA follow-up. Review of these cases is ongoing and approximately 80% complete.*

*With local IRB and HRPO approval Drs. True and Mosquera have each begun reviewing cases meeting the above three criteria. Dr. True is approximately 33% completed with review of cases meeting criteria 1 to 3 above, while Dr. Mosquera is approximately 25% completed. The first 160 cases from Dr. Mosquera are being cut and transferred to UM for staining at present.*

*Overall, these tasks are approximately 40% completed.*

- 3) Prospectively identify and review eligible biopsy cases
  - a. Prospectively identify and review biopsy cases (n=34) with discontinuous involvement (months 3-32).

- b. Prospectively identify and review biopsy cases (n=34) from pathology database with Gleason score 6 or 3+4=7 and 2-5 positive cores (months 3-32).

*All three sites have been identifying and reviewing biopsy cases as part of their routine clinical practice. At UM, we have been logging these cases and entering clinical information into our common database structure. We have identified a total of 25 discontinuously involved biopsies and 55 cases meeting criteria 3.b. UM cases were included in our initial manuscript of discontinuously involved cancer on biopsy (see below). UW and WCMC are including these cases as part of their formal review of cases meeting criteria in Specific Aim 1.2a-c.*

*These tasks are approximately 60% completed.*

- 4) Perform ERG/SPINK1 dual IHC
  - a. Perform dual ERG/SPINK1 IHC on retrospectively and prospectively identified cases (n=402) identified and reviewed above (months 6-32).
  - b. Evaluate dual ERG/SPINK1 IHC (months 7-32).
  - c. Scan 100 cases for evaluation by Drs. True and Mosquera (months 12-14).

*To save costs, all immunostaining from cases identified at the three institutions is being performed at UM. Staining of the UM and WCMC cohorts is ongoing and our initial findings have been published as described below. In our discontinuously involved cohort, discrepant (e.g. multiclonal) ERG/SPINK1 staining has continued to be observed in approximately 10-20% of cases. As described in our year 1 progress report and our publication, we have identified numerous cases where prospective identification of multiclonal foci would likely change management. A remarkable case evaluated during this funding period is shown in **Figure 1**, where discontinuous foci show distinct Gleason scores (4+3=7 on the left and 3+3=6 on the right). Without knowledge of multiclonality, this core would be graded as a 3+4=7. However, as shown in Figure 1, the foci show discrepant ERG status and thus represent independent foci of Gleason score 4+3=7 and 3+3=6, and combining the foci for tumor volume estimation and Gleason scoring would be inappropriate.*

*Likewise, in our first 78 evaluated cases with 2-5 involved cores of Gleason score 6 or 3+4=7 (cohort 2), we identified 17 discordant ERG/SPINK1 cases (21.8%), remarkably concordant with the 18% discordant rate in the 34 cases (unselected for Gleason score or number of positive cores) included in our preliminary data from a previous cohort. An example of discordantly staining cores from the same case is shown in **Figure 2**.*

*Importantly, all stained cases are being archived for scanning for review by Drs. True and Mosquera.*

*Overall, these tasks are approximately 20% completed.*

Specific Aim 2: Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy.

- 1) Input clinicopathological data into common database for cases stained and evaluated above (months 4-32).
- 2) Input ERG/SPINK1 dual IHC data into common database for cases stained and evaluated above (months 4-32).
- 3) Assess associations between extent tumor involvement and number of positive cores with and without multiclonality incorporation and parameters associated with significant pathology at prostatectomy (months 32-34)
- 4) Prepare manuscript on study (months 34-36)

*We have modified data fields from pre-existing databases at each institution to enable recording of common data elements and dual ERG/SPINK1 staining results.*

*Information for all stained UM cases has been entered into the local modified database. Information from additional UM cases and UW and WCMC cases (after HRPO approval) will be entered upon staining as described in Aim 1.*

*These tasks are approximately 20% completed.*

Specific Aim 3: Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction.

- 1) Input clinicopathological data into common database for cases stained and evaluated above (months 4-32).
- 2) Input ERG/SPINK1 dual IHC data into common database for cases stained and evaluated above (months 4-32).
- 3) Assess associations between Gleason score and tumor volume with and without multiclonality incorporation and PSA recurrence (months 32-34)
- 4) Prepare manuscript on study (months 34-36)

*We have modified data fields from pre-existing databases at each institution to enable recording of common data elements and dual ERG/SPINK1 staining results.*

*Information for all stained UM cases has been entered into the local modified database. Information from additional UM cases and UW and WCMC cases (after HRPO approval) will be entered upon staining as described in Aim 1.*

*These tasks are approximately 20% completed.*

**What opportunities for training and professional development has the project provided?**

Nothing to Report

**How were the results disseminated to communities of interest?**

We have published our first set of results from this proposal that report on the frequency of multiclonality in discontinuous biopsy cases.

Fontugne J, Davis K, Palanisamy N, Udager A, Mehra R, McDaniel AS, Siddiqui J, Rubin MA, Mosquera JM, Tomlins SA. Clonal evaluation of prostate cancer foci in biopsies with discontinuous tumor involvement by dual ERG/SPINK1 immunohistochemistry. *Mod Pathol*. 2016 Feb;29(2):157-65. doi: 10.1038/modpathol.2015.148. Epub 2016 Jan 8. PMID: 26743468 PMCID: PMC4732921

**What do you plan to do during the next reporting period to accomplish the goals?**

The major barrier to achieving our goals has been obtaining local IRB and HRPO approval from all three participating sites, which has now been completed. Review at all three sites is ongoing and cases from UM are being stained while those from UW and WCMC are being cut and transferred to UM for evaluation. Importantly, dual ERG/SPINK1 staining has been performed at UM and we are batching staining when large numbers of samples are ready to save on reagent costs. Additionally, Dr. Tomlins has reached out to other potential collaborators, such as Dr. Tarek Bismar of the University of Calgary, who may be able to contribute cases if additional cases are needed.

**IMPACT:**

**What was the impact on the development of the principal discipline(s) of the project?**

Nothing to Report

**What was the impact on other disciplines?**

Nothing to Report

**What was the impact on technology transfer?**

Nothing to Report

**What was the impact on society beyond science and technology?**

Nothing to Report

**CHANGES/PROBLEMS:**

**Changes in approach and reasons for change**

Nothing to Report

**Actual or anticipated problems or delays and actions or plans to resolve them**



As described above, we have had significant delays obtaining local IRB and HRPO for all three participating sites. We have not encountered additional problems beyond these approval issues, although review and evaluation of cases has been somewhat delayed.

**Changes that had a significant impact on expenditures**

Distribution of funds from UM to WCMC and UW was delayed while waiting for HRPO approval. Likewise, given the delay in accumulating cases and the somewhat short stability of some IHC components, we have delayed some antibody/staining components while waiting for case numbers to increase.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to Report

**PRODUCTS:**

**Publications, conference papers, and presentations**

As described above, we have published our first set of results from this proposal that report on the frequency of multiclonality in discontinuous biopsy cases.

Fontugne J, Davis K, Palanisamy N, Udager A, Mehra R, McDaniel AS, Siddiqui J, Rubin MA, Mosquera JM, Tomlins SA. Clonal evaluation of prostate cancer foci in biopsies with discontinuous tumor involvement by dual ERG/SPINK1 immunohistochemistry. *Mod Pathol*. 2016 Feb;29(2):157-65. doi: 10.1038/modpathol.2015.148. Epub 2016 Jan 8. PMID: 26743468 PMCID: PMC4732921

**Website(s) or other Internet site(s)**

Nothing to Report

**Technologies or techniques**

Nothing to Report

**Inventions, patent applications, and/or licenses**

Nothing to Report

**Other Products**

Nothing to Report

**PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

**What individuals have worked on the project?**

Name:	Scott Tomlins
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. Tomlins has led all aspects of the study as the PI, including directing database queries at UM, reviewing cases and over-seeing dual ERG/SPINK1 immunohistochemistry. Dr. Tomlins has also assisted in the IRB/DOD HRPO submissions for WCMC and UW.
Funding Support:	

Name:	Juan Miguel Mosquera
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. Mosquera has pursued local IRB approval and HRPO approval for the WCMC site and reviewed cases for transfer to UM.
Funding Support:	

Name:	Larry True
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. True has pursued local IRB approval and HRPO approval for the UW site and reviewed cases for transfer to UM .
Funding Support:	

Name:	Sumin Han
-------	-----------

Project Role:	Technician
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Dr. Han has led ERG/SPINK1 immunohistochemistry at UM.
Funding Support:	

Note: Connie Brenke, who performed staining (at less than 1 person month) in year 2, is no longer working on this project with staining being performed by Dr. Han.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Please see the Appendix for updated Other Support documents for Drs. Tomlins, Mosquera and True. New and Ended support is indicated for each investigator.

- **What other organizations were involved as partners?**

As in original submission

University of Washington  
1959 NE Pacific St  
Seattle, Washington 98036  
Collaborator (Dr. Larry True, Co-I)

Joan & Sanford Weill Cornell Medical College  
1300 York Ave  
New York, New York 10065  
Collaborator (Dr. Juan Miguel Mosquera, Co-I)

## **SPECIAL REPORTING REQUIREMENTS**

### **Collaborative Awards:**

N/A

### **Quad Charts:**

N/A

### **APPENDICES (see next page):**

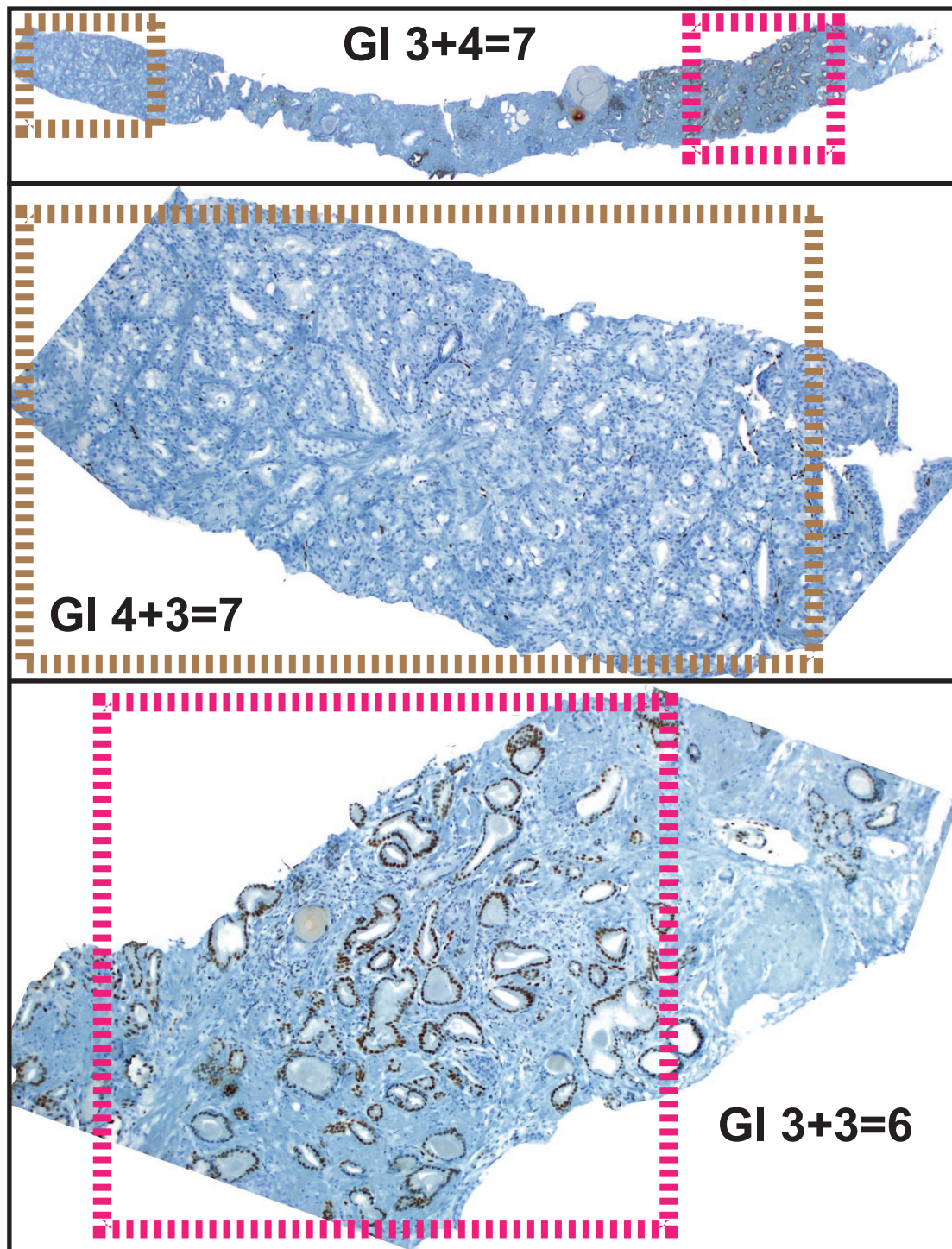
Figures 1 and 2

Updated Other Support for Dr. Tomlins

Updated Other Support for Dr. Mosquera

Updated Other Support for Dr. True

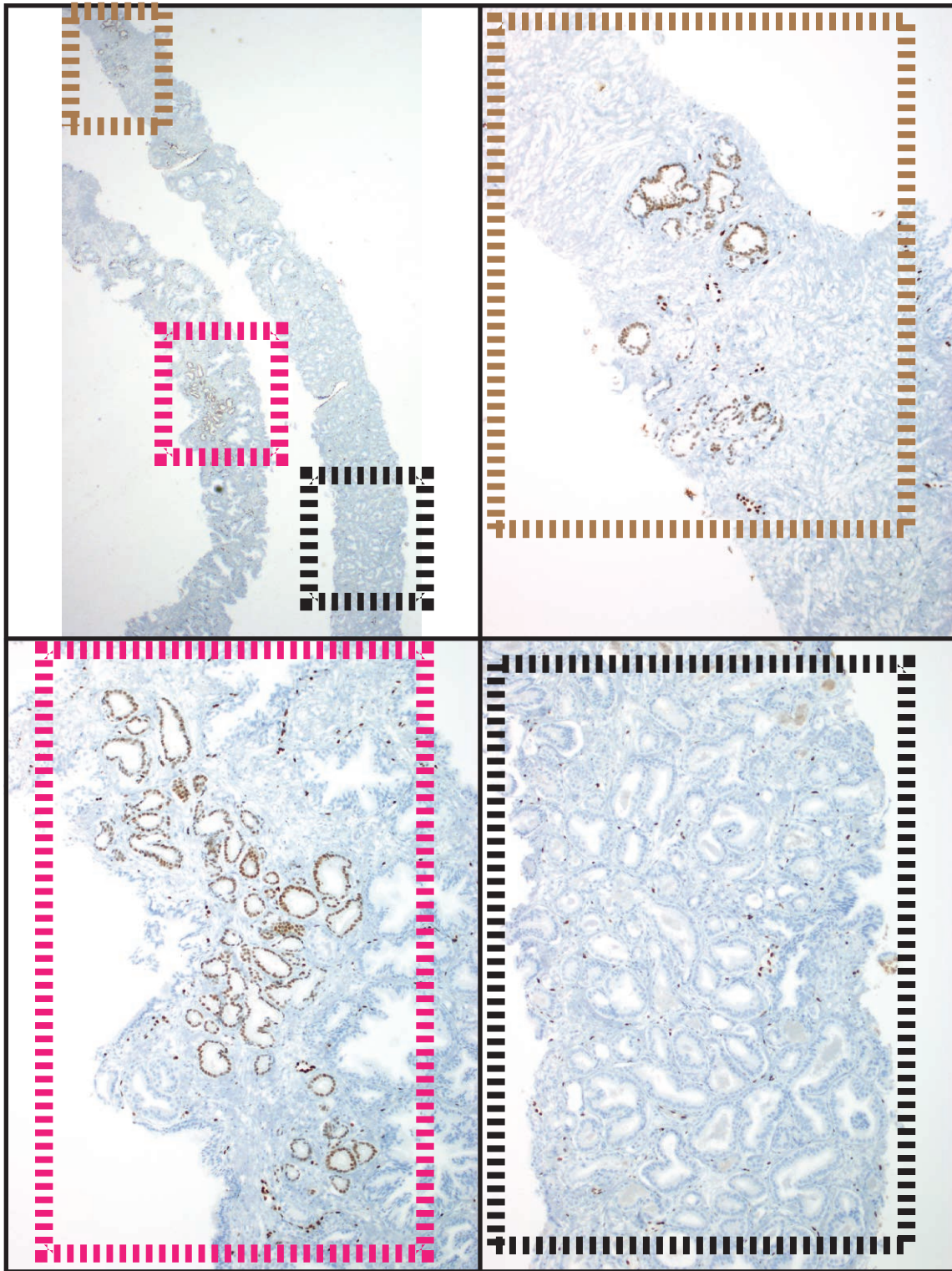
# Figure 1



**Figure 1. ERG/SPINK1 dual immunohistochemistry identifies multiclonal discontinuous involvement by foci of distinct Gleason scores.** In the top box, a prostate core discontinuously involved by foci of prostatic adenocarcinoma with Gleason score 4+3=7 (left, brown dashed box, middle box) and Gleason score 3+3=6 (right, magenta dashed box, bottom box) is shown. Per convention, these foci would be considered to represent the same tumor and the core would be reported as Gleason score 3+4=7 and involving 90% of the core. By dual ERG/SPINK1, the discordant staining (left focus ERG-/SPINK1- and right focus ERG+/SPINK1-) supports multiclonal disease, with the core involved by separate foci of focus of Gleason score 4+3=7 and Gleason score 3+3=6, each involving 15-20% of the core.



## Figure 2



**Figure 2. ERG/SPINK1 dual immunohistochemistry identifies multiclonal discontinuous involvement in two cores from the same case.** Two biopsy cores from the same case had Gleason score 3+3=6 prostatic adenocarcinoma, one with carcinoma involving 10% of one core (magenta dashed box, bottom left box), and the other was discontinuously involved by two foci together involving 80% of the core (by convention). Dual ERG/SPINK1 staining revealed discordant ERG/SPINK1 status between the cores (supporting multiclonal disease), as well as multiclonal disease in the discontinuously involved core. Hence, rather than both cores being involved by a single cancer focus, ERG/SPINK1 staining demonstrates the presence of at least two clonally distinct cancer foci.

## OTHER SUPPORT

### TOMLINS, SCOTT

#### ACTIVE

U01 CA179106 (Hadjiyski) 05/15/14 - 04/30/18 5%  
NIH \$14,033/yr salary support

***Biomarkers for Staging and Treatment Response Monitoring of Bladder Cancer***

Goal(s): The goal of this project is to develop effective decision support tools that merge image-based and non-image-based biomarkers to assist radiologists and oncologists in assessment of cancer stage and change as a result of treatment.

Specific Aims: To develop QIBC to assist radiologists in evaluation of bladder GTV on multimodality images (MM-bladder tumors); To develop decision support systems to assist clinicians in staging and monitoring of treatment response of bladder cancer by using image biomarkers, pathological information and diagnostic test results, and immunohistochemical biomarkers; To evaluate the effects of QIBC and CDSS-T on clinicians' inter-observer variability, efficiency and accuracy in estimation of bladder GTV and tumor treatment response by observer studies; To evaluate the CDSS-S and CDSS-T as clinical decision support tools for estimation of tumor treatment response in pilot clinical studies.

Role: Co-Investigator

Contact information at funding agency: Darayash Tata, NIH

PC13065 (PI: Tomlins) 09/01/14 – 08/31/17 7%  
Department of Defense \$125,000/yr

***Clonal Evaluation of Prostate Cancer by ERG/SPINK1 Status to Improve Prognosis Prediction***

Goal(s): Utilize ERG/SPINK1 status to assess the frequency of multiclonality in clinically relevant scenarios and to determine whether incorporating tumor clonality improves prognostic prediction.

Specific Aims: 1) Assess the frequency of multiclonality in clinically important scenarios using dual ERG/SPINK1 IHC; 2) Determine whether multiclonality assessment at biopsy improves prediction of pathology at prostatectomy; 3) Assess whether multiclonality assessment of index foci at prostatectomy improves outcome prediction

Contact information at funding agency: Theresa J. Miller, Ph.D , Phone: 301-619-6875;

[theresa.j.miller.ctr@mail.mil](mailto:theresa.j.miller.ctr@mail.mil)

5 P50 CA069568-15 (PI: Chinnaiyan) 09/01/14 - 08/31/19 12.5%  
NIH \$193,476/yr

***SPORE in Prostate Cancer***

Overview: This application consists of four multidisciplinary projects: Project 1: A Precision Medicine Approach to Elucidate Mechanisms of Progression and Resistance to Therapy in Advanced PCa; Project 2: Mechanisms of Sensitivity and Resistance to Cabozantinib in CRPC; Project 3: Development of Novel BET Bromodomain Inhibitors for the Treatment of Advanced PCa; Project 4: Development of IncRNAs as PCa Biomarkers in Urine. These projects are complemented by ongoing, successful Career Development and Developmental Research Programs.

Role: Co-Leader of Project 2

Contact Information at funding agency: Andrew Hruszkewycz, 301-496-8528, hruszkea@mail.nih.gov

R01CA183857 (PI: Tomlins) 04/3/14 - 02/28/19 19%  
NIH \$207,500/yr

***Exploiting drivers of androgen receptor signaling negative prostate cancer for precision medicine***

Goal(s): Identify novel potential drivers of AR- prostate cancer through sequencing xenografts and tissue samples. Qualify novel drivers of AR- prostate cancer through in vitro models. Develop novel treatment strategies for AR- and AR+ prostate cancer through in vivo models.

Specific Aims: 1) Identify novel potential drivers of AR- prostate cancer. 2) Qualify novel drivers of AR- prostate cancer through *in vitro* models. 3) Develop novel treatment strategies for AR- and AR+ prostate cancer through *in vivo* models exploiting AR- drivers.

Contact information at Funding Agency: Morrow, Charles, 301-451-4467, [morrowcs@csr.nih.gov](mailto:morrowcs@csr.nih.gov)

UM1HG006508 (PI: Chinnaiyan)

07/19/13 – 06/30/17

2%

National Institutes of Health

\$1,312,107/yr

***Exploring Precision Cancer Medicine for Sarcoma and Rare Cancers***

Goal(s): The overall goal of this project is to bring together expertise at the University of Michigan including clinical oncology, cancer genetics, genomic science/bioinformatics, clinical pathology, social and behavioral sciences, and bioethics in order to implement clinical cancer sequencing of patients with sarcomas and other rare cancers to enable the detection of clinically significant molecular lesions (point mutations, insertions/deletions, gene fusions and rearrangements, outlier expressed genes, and amplifications/deletions).

Specific Aims: Project 1: Clinical Genomic Study, 1) Accrue 500 patients with advanced or refractory rare cancer for participation in an integrated approach to Clinical Genomics; 2) Interpret results through a multi-disciplinary Sequencing Tumor Board and disclose results to patients and their physicians; 3) Measure the influence of sequence results provided to patients; 4) Determine the frequency of clinically significant germline mutations in patients undergoing comprehensive tumor sequence analysis.

Project 2: Sequencing, Analysis, and Interpretation of Sequencing Data; 1) Process and track specimens and ensure quality control; 2) Sequence tumor and germline biospecimens; 3) Analyze sequencing data to identify clinically significant variants; 4) Interpret and translate sequence variants into clinical oncology setting; 5) Assess and evaluate costs associated with clinical sequencing.

Role: Co-Investigator

Contact Information at funding agency: Harvey, Zephaun, [harveyz@mail.nih.gov](mailto:harveyz@mail.nih.gov), 301 435-7859

Award No. N/A (PI: Maher/Feng/Sharifi/Tomlins)

01/01/15 - 12/31/16

1%

Prostate Cancer Foundation

\$121,000/yr

***Identifying Early Biomarkers of Anti-Androgen Treatment Resistance and Lethal Prostate Cancer***

Goal(s): Radiation Therapy Oncology Group (RTOG) 96-01 represents a phase III trial of salvage radiation therapy (RT) alone versus combined therapy (androgen deprivation therapy [ADT] and RT). This represents a highly unique population of 771 patients with aggressive localized prostate cancer following standard treatment options with long-term clinical outcomes (median follow-up of 9 years). The overarching goal of this proposal is to leverage this unique patient population to explore the molecular underpinnings predictive of treatment response and associated with lethal disease.

Role: Co-PI

Contact information at Funding Agency: Audrey Gardner, [agardner@pcf.org](mailto:agardner@pcf.org)

Award No. N/A (PI: Rubin/Tomlins)

07/01/15 - 06/30/17

1%

Prostate Cancer Foundation

\$155,076/yr

***Integrative Genomics of Prostate Cancer Progression***

Goal(s): Retrospectively collect, review, and perform comprehensive molecular characterization on the original diagnostic biopsy or prostatectomy samples from men with castration resistant prostate cancer (CRPC) participating on the CRPC 500 trial to identify molecular determinants of prostate cancer progression.

Contact information at Funding Agency: Audrey Gardner, [agardner@pcf.org](mailto:agardner@pcf.org)

R01 CA181605 (PI: Nelson)	01/01/16 - 12/31/16	8%
NIH	\$80,000/yr	

***Non Invasive Biomarkers for Diagnosing Clinically Significant Prostate Cancer***

Goal(s): Test the hypothesis that biomarkers indicative of adverse prostate cancer behavior—Gleason grade, tumor volume and detrimental molecular alterations—can be reproducibly detected in the urine of men with prostate cancer; Determine whether initial sampling of a panel of urine biomarkers and the repeated assessment of a urine biomarker panel over time will associate with the presence of significant versus insignificant cancer in the prostate, and thus can be used in informing decisions for continuing surveillance or proceeding with definitive treatment.

Specific Aims: 1) Determine if PCA3 and TMPRSS2:ERG mRNA concentrations in urine associate with the presence or development of clinically-significant prostate cancer using longitudinal repeat assessments in men on Active Surveillance; 2) Evaluate a panel of long non-coding RNAs (lncRNAs) in tissue and urine for the detection of significant prostate cancer in men on Active Surveillance; 3) Define and evaluate a panel of Gleason Pattern-associated RNAs in tissue and urine for the detection of significant prostate cancer in men on Active Surveillance.

Role: Co-Investigator

Contact information at Funding Agency: Alexander Moreno, [amoreno@fhcrc.org](mailto:amoreno@fhcrc.org)

R01 DK106618 (PI: Rainey and Tomlins)	03/01/16-02/28/20	10%
NIH	\$299,867/yr	

***Adrenal Origins of Aldosterone Excess***

Goals(s): This proposal will test the hypotheses that most adults have neoplastic cells bearing “first hit” somatic mutations that cause renin-independent aldosterone production. Primary aldosteronism and hypertension result from additional “multi-hit” mutations that increase cell proliferation, tumor development and pathologic levels of aldosterone. We will test the hypotheses that APCC are dysplastic cells bearing somatic gene mutations that activate aldosterone production and that APA have the same mutations seen in APCC, but exhibit additional mutations that cause cell proliferation and tumor development.

Specific Aims: 1) Define the somatic mutations found in normal adrenals that exhibit adrenal aldosterone-producing cell clusters (APCC). 2) Define the somatic gene mutations present in aldosterone-producing adenomas (APA).

Contact Information at Funding Agency: Saul N Malozowski Email: [malozowskis@extra.niddk.nih.gov](mailto:malozowskis@extra.niddk.nih.gov), Phone: (301) 451-4683

PC141474 (PI: Tomlins)	09/30/15-09/29/18	8%
DOD	\$169,574/yr	

***Comprehensive Molecular Profiling of African-American Prostate Cancer to Inform on Prognosis and Disease Biology***

Goal(s): Perform comprehensive expression profiling of prostate cancer (PCa) in AA men to assess the performance of PCa prognostic gene expression signatures and characterize known and novel gene fusions, mutations and copy number alterations.

Specific Aims: 1) Perform comprehensive expression profiling of PCa in AA men to assess the performance of PCa prognostic gene expression signatures. 2) Characterize known and novel PCa gene fusions in AA men. 3) Characterize known and novel PCa mutations and CNAs in AA men to develop an integrated prognostic signature.

Contact Information at funding agency: Tom Winter, [thomas.s.winter2.civ@mail.mil](mailto:thomas.s.winter2.civ@mail.mil), (240) 357-1590.

R01 CA196619 (PI: Cho)	05/01/16-04/30/19	4%
NIH	\$304,358/yr	



### ***Credentialing Ovarian Cancer Models in the Context of the Dualistic Pathway Paradigm***

Goal(s): Enhance the applicability of mouse models for translational research using novel genetically engineered mouse models (GEMMs). We have developed a new GEMM that employs the Ovgp1 promoter to direct expression of Tamoxifen (TAM)-inducible Cre recombinase in the fallopian tube epithelium (FTE). Ovgp1-iCreERT2 mice that also carry floxed alleles of tumor suppressor genes that are characteristically inactivated in ovarian endometrioid carcinoma (OEC, prototypical Type I tumor) and high grade serous ovarian carcinomas (HGSC, prototypical Type II tumor) can be induced to form tumors in the FTE following treatment with TAM, or tumors arising in the ovarian surface epithelium (OSE) following ovarian bursal injection of adenovirus expressing Cre.

Specific Aims: 1) To credential GEMMs of ovarian cancer (OvCa) arising from FTE- transformation as superior to those arising from OSE-transformation in terms of their morphological and molecular similarity to their human OvCa counterparts; and 2) To test a new tool strain for early detection of oviductal HGSCs based on cervical-vaginal lavage (murine Pap test).

Role: Co-Investigator

Contact Information at funding agency: Mariam Eljanne, Email: [eljannem@mail.nih.gov](mailto:eljannem@mail.nih.gov), Phone: 301-443-3612

U01CA214170 (PI:Chinnaiyan and Tomlins)

09/01/16-08/31/21

NIH

\$370,065/yr

### **Discovery and qualification of transcriptomic biomarkers for the early detection of aggressive prostate cancer**

Goal(s): Nominate and develop transcriptomic biomarkers as predictors of aggressive prostate cancer both at and prior to diagnosis.

Specific Aims: 1) Identify and develop assays to study novel aggressive prostate cancer-associated transcriptomic alterations from our MiTranscriptome analysis. 2) Characterize transcripts from Aim 1 as tissue based aggressive prostate cancer biomarkers using individual in situ hybridization assays and a multiplexed next generation sequencing (NGS). 3) Characterize transcripts from Aim 1 as non-invasive, urine-based aggressive prostate cancer early detection biomarkers through collaboration with our industry partner and multiplexed NGS.

Contact information at Funding Agency: Sudhir Srivastava, 240-276-7028, [ss1a@nih.gov](mailto:ss1a@nih.gov)

## **PENDING**

(PI Rubin)

04/01/17-03/31/22

5%

NIH

\$97,336/yr

### ***Towards Understanding the Genomic Heterogeneity of Metastatic Prostate Cancer (SPORE Project)***

Goal(s): As part of the Weill Cornell Medical College S.P.O.R.E., this project aims to assess a large cohort of paired primary ADT-naïve and metastatic CRPC specimens to understand and exploit the molecular mediators of PCa progression to inform on optimal clinical pathologic practice, identify biomarkers, and inform on disease biology.

Specific Aims: 1). Collect and histologically characterize original primary ADT-naïve specimens from patients enrolled in the CRPC 500 trial. 2). Determine the molecular landscape of multiple tumor foci from the original ADT-naïve CRPC 500 specimens through DNA and RNA sequencing. 3). Identify molecular mediators of PCa progression and track the progressing clone through an integrative molecular profiling analysis of paired primary ADT-naïve and CRPC specimens

Role: Project Co-Leader (Co-Investigator)

Contact information at Funding Agency: Seran Lee-Johnson, [sel2016@med.cornell.edu](mailto:sel2016@med.cornell.edu), (646) 962-6998

PC151032 (PI: Cooney)

09/30/18-09/29/19

3%

DOD

\$26,743/yr

***Characterizing the Genetic Landscape of Prostate Cancer in Young African American Men***

Goals(s): The underlying hypothesis of this proposal is that African American men with early-onset prostate cancer are more likely to harbor germline variants that increase the risk of developing clinically significant prostate cancer, as well as novel driving somatic alterations. In this proposal, NGS approaches will be used to analyze germline DNA from 750 African American men with clinically significant prostate cancer diagnosed before age 60 years of age focusing on genes already known to be mutated in the germline or tumor of men with prostate cancer or other cancers as well as genes in functional pathways of interest (i.e. hormone biosynthesis and signaling and DNA damage repair).

Specific Aims: 1) Collect germline DNA from 750 young African-American men diagnosed with clinically significant prostate cancer. 2) Perform germline sequencing of candidate genes on the cohort to identify to identify deleterious variance. 3) Perform targeted next generation sequencing on tumor samples from the subset of the men with germline DNA mutations.

Role: Co-Investigator

Contact information at Funding Agency: Christine LaSalle, [christine.lasalle@hsc.utah.edu](mailto:christine.lasalle@hsc.utah.edu), (801) 585-2734

**ENDED WITHIN THE LAST 5 YEARS**

Award No. N/A (PI: Knudsen)

10/15/12 – 10/15/14

2%

Movember-Prostate Cancer Foundation

\$250,000/yr

Challenge Award

***Interrogating DNA Repair Defects to Improve Management of Advanced Prostate Cancer***

Goal(s): The overall goal of this proposal is to identify therapeutic strategies to target DNA damage response pathway alterations in patients with advanced prostate cancer.

Specific Aims: 1) To identify and comprehensively determine the frequency of aberrations in DNA damage response pathways at different stages of prostate carcinogenesis; 2) To determine the clinical relevance of these DNA repair defects; 3) To evaluate the functional and biological consequences of these DNA repair defects and identify novel therapeutic strategies that will benefit patients suffering from such cancers.

Role: Co-Investigator

Contact Information at funding agency: Audrey Gardner, PCF Applications ([applications@pcf.org](mailto:applications@pcf.org))

Award No. N/A (PI: Knudsen/Feng/Tomlins)

12/01/13 - 11/30/15

2.5%

Prostate Cancer Foundation

\$200,000/yr

***Targeting DNA Repair Alterations To Improve Treatment for Advanced Prostate Cancer***

Goal(s): Comprehensively interrogate DNA repair alterations in both AR-positive and AR-negative CRPC to develop novel biomarkers and therapeutic strategies with the goal of improving outcomes for patients with these aggressive diseases

Specific Aims: 1) Determine the molecular and cellular consequence of tumor-associated DNAPK dysregulation; 2) Assess the impact of targeting DNAPK and the DDR on tumor progression & therapeutic response; 3) Targeting AR-mediated DNA repair through the requisite cofactor USP22; 4) Profiling DNA repair alterations in AR-negative, late stage disease.

Role: Co-PI

Contact Information at funding agency: Audrey Gardner, PCF Applications ([applications@pcf.org](mailto:applications@pcf.org))

Award No. N/A (Dream team leader: Chinnaiyan)

08/01/12 – 07/31/15

2.5%

AACR Stand up to Cancer and

\$808,511/yr

Prostate Cancer Foundation Dream Team

***Precision Therapy of Advanced Prostate Cancer***

Goal(s): The overall goal of this proposal is to catalyze the interaction of a multi-disciplinary team of investigators, with a track record of accomplishments in prostate cancer research, to work together on the challenging problem of metastatic castration resistant prostate cancer (CRPC).

Specific Aim(s): 1) Establish a multi-institutional infrastructure incorporating 5 leading prostate cancer clinical sites, 2 sequencing and computational analysis sites, linked with appropriate sample and data coordination; 2) Establish a prospective cohort of 500 patients (the “CRPC 500”) utilizing the multi-institutional infrastructure to support the clinical use of integrative prostate cancer sequencing, analysis, and clinical trial decision making; 3) Conduct parallel, preclinical *in vivo* functional studies of resistance biomarkers and of SU2C-PCF sponsored combination therapies; 4) Identify molecular determinants of abiraterone sensitivity and acquired resistance in patients; 5) Conduct clinical trials of novel combinations targeting AR and/or the PTEN pathway, based on existing preclinical data and an understanding of resistance mechanisms; 6) Identify molecular determinants of sensitivity and acquired resistance to PARP inhibitors in patients.

Role: Co-Investigator

Contact Information at funding agency: Frederic Biemar, ([frederic.biemar@aacr.org](mailto:frederic.biemar@aacr.org)), (215) 446-7261

PC120464 (PI: Cooney)

09/30/13 - 09/29/16

12%

Department of Defense

\$125,060/yr

***High throughput sequencing of germline and tumor from men with early-onset, metastatic prostate cancer***

Goal(s): To perform next generation sequencing on germline DNA, prostate cancer, and normal prostate tissue on samples from men with early-onset, clinically significant disease.

Specific Aims: 1. To identify and clinically characterize a set of 20 men who present with Stage 4 (Tx N1 and/or M1) prostate cancer at an early age defined as at or before age 60, and 2. To interrogate the germline exome and tumor exome/transcriptome from 20 men with early-onset Stage 4 prostate cancer to identify novel molecular alterations that may contribute to the early-onset, aggressive prostate cancer.

Role: Co-Investigator

Contact Information at Funding Agency: Kathy E. Robinson, Grants Officer, Us Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick Md 21702-5014

PC121111 (PI: Scher, H.)

10/01/13 – 09/30/16

2%

Department of Defense

\$300,000/yr

***Toward the Practice of Precision Medicine: A Biomarker Validation Coordinating Center***

Goals(s): Establish Multicenter Validation of Biomarker Assays for Clinical Management of Prostate Cancer and validate TMRSS2:ERG assays; Validate the utility of the TMRSS2:ERG TMA assay for the non-invasive detection of clinically significant prostate cancer in urine; Validate the ERG rearrangement FISH assay on tissues and determine the prevalence of ERG rearrangements in isolated precursor and diagnostically challenging lesions

Specific Aims: 1) To cross-validate an initial set of assays for biomarkers corresponding to the AR and PI3K/PTEN axes ready for near-term filing with the FDA for use in prospective integral biomarker-driven trials in prostate cancer; 2) To use the centralized infrastructure of the Assay Validation Coordinating Center to cross-validate additional assays for biomarkers identified via established and emerging discovery platforms (i.e., NCI Prostate Cancer SPOREs, PCF, SU2C, and TCGA) for use in prospective integral biomarker-driven trials in prostate cancer.

Role: Co-Investigator

Contact Information at Funding Agency: Kathy E. Robinson, Grants Officer, Us Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick Md 21702-5014

## **OVERLAP**

There is no scientific or budgetary overlap.

**Mosquera, Juan M.**

CURRENT

**U01 CA162148 (Garraway, L.)**

*Systemic Genetic Characterization of African American Prostate Cancer*

0.6 calendar

National Institute of Health

Grants Officer: N/A

7/1/12-6/30/17

\$40,000

The over-arching goal of this proposal is to undertake a definitive somatic genetic and functional characterization of African-American prostate cancer.

Aim 1. Design and validation of hybrid capture-based genomic profiling protocol to genetically characterize African American prostate cancer tumor samples

Aim 2. Profiling of a cohort of African American prostate cancer samples

Aim 3. Functional and mechanistic studies of operant signaling pathways in African American cell lines in vitro

**R01 CA184712 (Rubin, M / Lin, D.)**

*Precision Medicine Approach to Prostate Cancer Active Surveillance*

1.8 calendar

National Institute of Health

Grants Officer: Sarah E. Scharf; email: [sarah.scharf@nih.gov](mailto:sarah.scharf@nih.gov); phone: 240-276-5472

8/1/14-7/31/19

\$550,815

The goal of this project is to confirm a novel panel of tissue-based biomarkers to determine the presence of or progression to aggressive disease in early stage PCa and prove that these biomarkers will reliably predict PCa progression and/or under-staging and grading

Aim 1. Confirm a novel panel of tissue-based biomarkers to determine the presence of or progression to aggressive disease.

Aim 2. Evaluate emerging tissue-based biomarkers for aggressive PCa in men on AS.

**R01 CA179100-01A1 (Rickman)**

*Mechanistic Insights Underlying ERG-induced Taxane Resistance in Castration-Resis*

0.36 calendar

National Cancer Institute (NIH)

Grants Officer: Suzanne L. Forry; email: [forryscs@mail.nih.gov](mailto:forryscs@mail.nih.gov) ; phone: N/A

04/11/14-02/28/19

\$253,027

Mechanistic Insights Underlying ERG-induced Taxane Resistance in Castration-Resistant Prostate Cancer  
The goal of this project is to understand the mechanism influencing ERG over-expression and resistance to taxane-based therapies in patients with metastatic castration resistant prostate cancer.

Aim 1. To investigate the non transcriptional mechanism by which ERG mediates resistance to taxanes.

Aim 2. To investigate the transcriptional mechanism

Aim 3. To determine the clinical impact of ERG over-expression on taxane sensitivity and resistance in CRPC patients.

**U01 CA086402 (Thompson, L.)**

*Biomarkers and clinical parameters associated with Gleason score upgrading*

1.2 calendar

National Institute of Health

Grants Officer: Chris Green; email: [greenc@uthscsa.edu](mailto:greenc@uthscsa.edu); phone: N/A

7/1/14-3/31/19

\$64,897

Project Goals: To grade and stage, tumor volume, presence of perineural and/or angiolymphatic invasion and margin status will also be recorded. Each individual tumor nodule will be mapped in prostatectomy specimens, and provided its own Gleason score and pathologic tumor (pT) stage.

**W81XWH-14-1-0466 (Tomlins)**

*Clonal Evaluation of Prostate Cancer by ERG/SPINK1 Status to Improve Prognosis Prediction*

0.96 calendar

United States Dept. of Defense

Grants Officer: Emily Tran; email: [tranc@mail.nih.gov](mailto:tranc@mail.nih.gov); Phone: 240-276-6324

Goal(s): Utilize ERG/SPINK1 status to assess the frequency of multiclonality in clinically relevant scenarios and to determine whether incorporating tumor clonality improves prognostic prediction.

Specific Aims: To develop QIBC to assist radiologists in evaluation of bladder GTV on multimodality images (MM-bladder tumors); To develop decision support systems to assist clinicians in staging and monitoring of treatment response of bladder cancer by using image biomarkers, pathological information and diagnostic test results, and immunohistochemical biomarkers; To evaluate the effects of QIBC and CDSS-T on clinicians' inter-observer variability, efficiency and accuracy in estimation of bladder GTV and tumor treatment response by observer studies; To evaluate the CDSS-S and CDSS-T as clinical decision support tools for estimation of tumor treatment response in pilot clinical studies.

PENDING

**P50 CA211024 (Rubin)**

*Weill Cornell Medicine (WCM) SPORE in Prostate Cancer*

0.6 calendar

National Institutes of Health

07/01/2017-6/30/2022

\$1,822,680

The goal of this project is to take a novel precision medicine approach to PCA patient care, by aligning translational research goals with the care of men across the PCA spectrum. The WCM SPORE will be a major hub for paradigm-shifting translational research, which will establish new approaches to PCA, which will result in improved patient survival and quality of life.

Aim 1. Develop accurate biomarkers to assess the risk of PCa disease progression using genomic and liquid biopsy approaches (Projects 1 and 3).

Aim 2. Develop new therapeutic approaches for clinically localized and CRPC that are hypothesis-driven, based on newly acquired knowledge of PCa biology and genomic, and represent a paradigm shift in treatments (Projects 2, 3, and 4).

Aim 3. Leverage existing and expand new infrastructure for the successful translation of pre-clinical studies into the clinic.

Aim 4. Train the next generation of PCa investigators

COMPLETED

**AACR SU2C Dream Team (Chinnaiyan, A. / Sawyers, C.)**

*Precision Therapy of Advanced Prostate Cancer*

1.2 calendar

American Association for Cancer Research

Grants Officer: Karen Giles; email: [kargiles@umich.edu](mailto:kargiles@umich.edu); phone: 734-763-3821

7/1/12-6/30/16

\$125,833

Project Goals: To examine the functional relevance of 5-10 candidate genes implicated by prostate cancer somatic mutations, develop companion functional approaches for the analysis of DNA and RNA sequencing and determine key targetable genes associated with prostate cancer.

**Starr Foundation Grant, I7-A722 (Chen, Y. / Rubin / Carver, B. / Beltran, H.)**

*Co-clinical trials using organoids for patients with advanced prostate cancer*

0.12 calendar

Starr Foundation Grant

Grants Officer: Sylvie LeBlanc; email: [leblancs@mskcc.org](mailto:leblancs@mskcc.org); phone: 212-639-8489

1/1/14-12/31/15

\$276,500

This project will create organoid lines from advanced prostate cancer patients to generate mutational and copy number data of each organoid line, determine whether *in vitro* sensitivity can predict for patient response, and generate potential biomarkers.

Aim 1. Generate clinically well-annotated organoid lines that accurately recapitulate the clinical and molecular diversity of abiraterone-resistant CRPC and NEPC

Aim 2. Characterize the mutational profile and copy number profile of each organoid line

Aim 3. Determine the *in vitro* drug sensitivity profile of organoid lines and correlate with patient response

**R01 CA179100 (Rickman)**

*Mechanistic Insights Underlying ERG-induced Taxane Resistance in Castration –Resistant Prostate Cancer*

0.36 calendar

National Institute of Health

Grants officer: Sarah M. Lee; 240-276-6280; [Sarah.Lee@nih.gov](mailto:Sarah.Lee@nih.gov)

04/11/14-02/28/19

\$253,027

Aim: To characterize the mechanism underlying ERG-induced taxane resistance in castrate resistant prostate cancer



**TRUE, Larry. D.**  
**ACTIVE**

2 P50 CA97186 (Nelson) 9/1/13-8/31/18 0.84 calendar  
NIH \$1,635,621

*Pacific Northwest Cancer SPORE*

**Core B: Biospecimen Core**

The Specimen Core provides part of the infrastructure support for Projects 1-4, as well as future pilot and developmental projects. It has been designed to meet the needs of these projects, plus serve as a stand-alone system of specimen collection, storage, distribution and related clinical/research information dissemination that is based on over two decades of experience.

Role: Dr. True will serve as the Pathologist and Co-Director of Core B.

Sponsor Contact: Peter Nelson, M.D., Fred Hutchinson Cancer Research Center (FHCRC), 1100 Fairview Avenue N., MS: J6-500, PO Box 19024, Seattle, WA 98109-1024, [pnelson@fhcrc.org](mailto:pnelson@fhcrc.org)

R01 CA176844-01 (Vasioukhin) 05/01/13 - 03/31/18 0.72 calendar  
NIH \$132,130

*The Hippo Pathway in Prostate Gland Homeostasis and Prostate Cancer*

This project hypothesizes that biomarkers of disease aggressiveness and prognosis can be measured in early stage prostate cancer and that these biomarkers will aid not only in choosing the initial course of therapy but also in decision-making during AS (Active Surveillance). The project proposes to interrogate a large multi-institutional cohort of men undergoing AS to confirm a platform of tissue and urine-based biomarkers that will reliably predict prostate cancer progression and or under-staging and –grading, thus determining patients who may avoid radical treatment, concurrently identifying men who may benefit from early treatment rather than active surveillance.

Role: Co-I

Sponsor Contact: James Pendleton, Fred Hutchinson Cancer Research Center (FHCRC), 1100 Fairview Avenue N., PO Box 19024, Seattle, WA 98109-1024, [jpendlet@fhcrc.org](mailto:jpendlet@fhcrc.org)

P01 CA163227 (Balk) 5/1/13-4/30/18 0.696 calendar  
NIH \$160,000

*Androgen Receptor Action In Castration Resistant Prostate Cancer*

**Core C: Biospecimen Core**

The major goal of the Biospecimen Core is to provide a well-organized and standardized system of specimen collection, storage, distribution and related clinical/research information dissemination that is based on over two decades of experience. The Core will ensure consistency and quality assurance in the pathological analysis of tissue specimens. It will maintain a large series of prostate cancer xenograft lines developed by Core investigators, which will be used for proposed studies by the P01 investigators.

Role: Co-I

Sponsor Contact: Julianne Carty, Harvard University, 330 Brookline Ave. E/CLS 650, Boston, MA 02215, 617-735-2002, [jcarty@bidmc.harvard.edu](mailto:jcarty@bidmc.harvard.edu)

PC 130652 (Tomlins) 9/30/14-9/29/17 0.936 calendar  
DOD \$22,148

*Clonal evaluation of prostate cancer by ERG/SPINK1 status to improve prognosis prediction*

The objectives will be to retrospectively and prospectively identify cases for cohorts 1-3. Dr. True will be responsible for performing and evaluating ERG/SPINK1 dual IHC stains on 300 cases. He will also be responsible for transferring the remaining cases/sections to Dr. Tomlins at UMHS and evaluating ERG/SPINK1 dual IHC stains on 100 cases stained at UMHS. He will also work with co-investigators at UMHS and Cornell in study design, data analysis and interpretation, and in manuscript preparation.

Role: Co-Investigator

Sponsor Contact: CDMRP, (301)682-5507, [help@cdmrp.org](mailto:help@cdmrp.org)

Parent Institution: University of Michigan

W81XWH1410595 (Lin)

9/30/14-9/29/17

1.2 calendar

DOD

\$77,161

*Biomarkers for Early Detection of Clinically Relevant Prostate Cancer: a Multi-Institutional Validation Trial*

Dr. True will be responsible for reviewing slides of prostate needle biopsies and characterizing the prognostic pathologic parameters in biopsies of participants in the PASS study. He will also identify areas of cancer for tissue samples used in Aim 1 of the project.

Role: Co-Investigator

Sponsor Contact: CDMRP, (301)682-5507, [help@cdmrp.org](mailto:help@cdmrp.org)

Parent Institution: Fred Hutchinson Cancer Research Center

W81XWH-15-1-0430 (Nelson)

7/1/15-6/30/18

2% effort

DOD

\$16,630

*Minimally-Invasive Assessments of Prostate Cancer Molecular Heterogeneity to Direct Precision Therapy*

Dr. True will assist in the acquisition and assessment of tumors acquired from men with advanced prostate cancer, evaluate tumor purity, and assist with evaluations of tumor heterogeneity by histology and immunohistochemical methods.

Role: Co-Investigator

Sponsor Contact: CDMRP, (301)682-5507, [help@cdmrp.org](mailto:help@cdmrp.org)

Parent Institution: Fred Hutchinson Cancer Research Center

W81XWH-14-2-0183 (Morrissey)

9/30/14-9/29/17

9.6 calendar

DOD

\$173,181

*Prostate Cancer Biorepository Network*

Dr. True participates in The Prostate Cancer Biorepository Network (PCBN). The goal of PCBN is to maintain and expand the current biorepository with high quality, well-annotated specimens that meet the critical needs of the prostate cancer research community, and which are obtained using optimized and standardized protocols.

Role: Co-Investigator

Sponsor Contact: CDMRP, (301)682-5507, [help@cdmrp.org](mailto:help@cdmrp.org)

## **ENDED SINCE LAST SUBMISSION:**

W81XWH13-2-0070 (Scher)

9/30/13-9/26/16

DOD

\$474,348

*Toward the Practice of Precision Medicine: Multicenter validation of Biomarker Assays for Clinical Management of Prostate Cancer*

*UW Subaward:*

\$103,827

1.8 calendar

The goal of this proposal is to revolutionize the clinical management of prostate cancer by cross-validating assays of integral biomarkers for prostate cancer that can be used in prospective, biomarker-driven clinical trials. This will be accomplished by facilitating critical collaboration between multidisciplinary teams of investigators at multiple institutions in order to 1) develop a pipeline of biomarkers prioritized for assay development, 2) determine the appropriate platform(s) for analysis, and 3) systematically address the preanalytical, analytical, and post-analytical variables including data redaction to validate and conduct tissue based assays in a CLIA environment.

Role: Co-I

Sponsor Contact: CDMRP, PCRP, (301) 619-7079, [cdmpr.pa@amedd.army.mil](mailto:cdmpr.pa@amedd.army.mil)

Parent Institution: Memorial Sloan-Kettering Cancer Center; Award Administrator: Michael McGregor, [mgregom@mskcc.org](mailto:mgregom@mskcc.org)



*Early Detection Research Network: Biomarker Developmental Laboratories* 9/22/10 – 6/30/15  
NIH (2U01CA111244-06) Liu, A., PI \$1,411,642 (DC/IDC whole period for all entries)  
0.24 calendar

This is the continuation of our participation in The Early Detection Research Network (EDRN) with the goal that our gene expression findings in prostate cancer and bladder cancer can be translated into practical clinical tests for timely cancer detection and risk assessment (disease stratification). Our work continues to analyze prostate and bladder cancer molecular and cellular signatures that include secreted and cell surface proteins found in voided urine. We measure these proteins by proteomics technologies, mass spectrometry, or ELISA to derive a viable urine test that can be developed for detecting these urologic cancers.

Sponsor Contact: Jacob Kagan, Ph.D., Division of Cancer Prevention, NCI, NIH, 6130 Executive Boulevard, EPN Rom 3147, MSC 7362, Rockville, MD 20852-73642, [kaganj@mail.nih.gov](mailto:kaganj@mail.nih.gov)

Role: Co-I

*Mechanisms and Markers of Prostate Cancer Metastases* 7/1/09-7/31/14 1.8 calendar  
NIH (2 P01 CA085859) Vessella, R., PI \$1,786,571

The major goal of this award is to continue studies on prostate cancer (CaP) metastasis, especially focusing on the dissemination and growth of CaP in bone. This effort has coordinated much previous work from a variety of sources within the UW and is multi-disciplinary, incorporating cancer and bone biology, cancer endocrinology, pathology and genomics. Institutional partners include the FHCRC and the UW Institute of Stem Cell Sciences.

*Core A: Tissues/Sera/Models* \$172,873

The major function of this core is to provide infrastructure support as follows: 1) Specimen acquisition, processing, storage and accession, 2) RT-PCR Immunohistochemistry and in situ hybridization services, 3) PSA and other immunoassay services, 4) tissue culture services, 5) CaP and control xenograft maintenance plus perform all xenograft studies.

Sponsor Contact: Suresh Mohla, Ph.D., Chief, Tumor Biology and Metastasis Branch, Division of Cancer Biology, NCI, NIH, Executive Plaza North, Room 5038, Rockville, MD 20852-7364, [mohlas@mail.nih.gov](mailto:mohlas@mail.nih.gov)

Role: Co-I